

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

In The Name Of ALLAH

The Most Gracious, The Most Merciful





Armed Forces College of Medicine AFCM





Drugs used to treat bronchial asthma and COPD (2)

***Prof. Dr/ Omayma
Khorshid***



INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Classify the drugs used in long term control of bronchial asthma
2. Explain the mechanism of action and adverse effects of inhaled corticosteroid, leukotriene modifiers.



Long-term control

Anti-Inflammatory• Drugs

.Corticosteroids -1

Leukotriene- -2

.modifiers

Mast Cell -3

.Stabilizers



CORTICOSTEROIDS

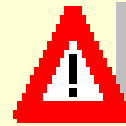
- Inhaled corticosteroid (ICS) are the drugs of choice for long-term control in patients with any degree of persistent asthma.
- Corticosteroid therapy directly targets underlying airway inflammation by:
 - ↓ Production of inflammatory cytokines as IL1,2,3,4- TNF.
 - ↓ Phospholipase A2 ↓ arachidonic acid synthesis ↓ products of arachidonic acid as leukotrienes.
 - ↓ Eosinophilic and lymphocytic airway mucosal inflammation in the airways
 - Antibody formation and antigen antibody reaction.

N.B: ICS Potentiate the effects of $\beta 2$ agonists and protect β receptor

CP module

9/11/2





Corticosteroids



Lipocortin



Phospholipase A₂

Phospholipid

\$



CORTICOSTEROI **DS**

1- Inhalation: For long-term control of bronchial asthma

✓ **inhalation of lipid soluble corticosteroids**
such as :

***beclomethasone, fluticasone,
budesonide & Ciclesonide***

Recommended and the preferred method:

as it avoids systemic adverse effects o
corticosteroids



- **To be effective in controlling inflammation, Inhaled corticosteroid (ICS) must be used regularly**
- **After several months of regular use, ICS reduce the hyperresponsiveness of the airway smooth muscle to a variety of bronchoconstrictor stimuli, such as:**
 - **Allergens**
 - **Irritants**
 - **Cold air**
 - **Exercise**



2- Systemic:

- ✓ In ***acute severe asthma (IV infusion)***
- ✓ when inhaled corticosteroids with other antiasthmatics are not enough to control symptoms

Dosage forms of Systemic corticosteroid

- ✓ **Oral** : e.g Prednisolone.
- I.V** methylprednisolone sodium succinate
OR
hydrocortisone sodium succinate .

Systemic therapy can be discontinued in 7-10 days

CP module

To switch patients from oral to inhaled

corticosteroid



Side Effects Of Inhaled Corticosteroids

ICS deposition on the oral and laryngeal mucosa can cause:

.Oropharyngeal Candidiasis (Thrush)
(due to local immune suppression)



.2 - Dysphonia □ Change in voice□

N.B

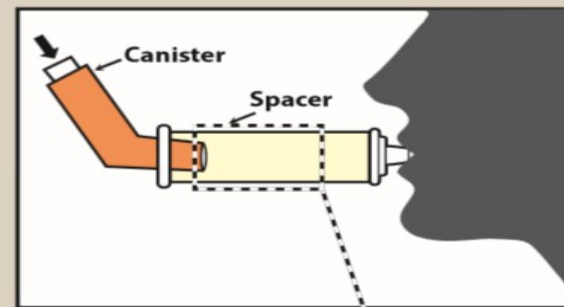
Most of these side effects can be avoided
by the use of **spacers or **rinsing the mouth****



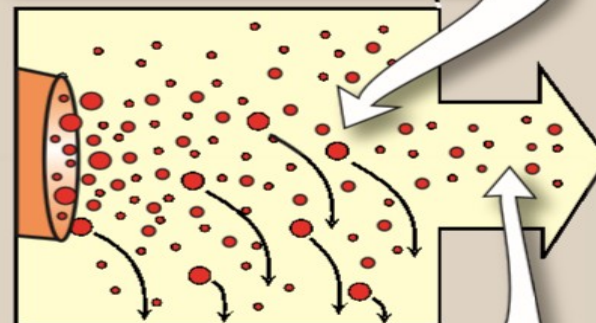


<http://adamimages.com/Illustration/SearchResult/1/spacer>

CP module



Large particles of aerosol are deposited in the chamber before the patient inhales.



Inhaled aerosol is enriched in small particles that more readily travel to the small airways.

Figure 29.7

Effect of a spacer on the delivery of an inhaled aerosol.

Whalen, K., Finkel, R., & Panavelil, T. A. (2015) Lippincott's Illustrated Reviews: Pharmacology (6th edition.). Philadelphia: Wolters Kluwer

9/11/2



Ciclesonide:

- low molecular weight ICS → high lung deposition.
- Once / day
- **Prodrug activated by cleavage by esterases in bronchial epithelial cells.**
- **less dysphonia and candidiasis than other**



1-Which of the following drugs is an inhaled corticosteroid and prodrug activated by cleavage by esterases in bronchial epithelial cells?

- a) Budesonide
- b) Fluticasone
- c) Beclomethasone
- d) Ciclesonide
- e) Bambuterol



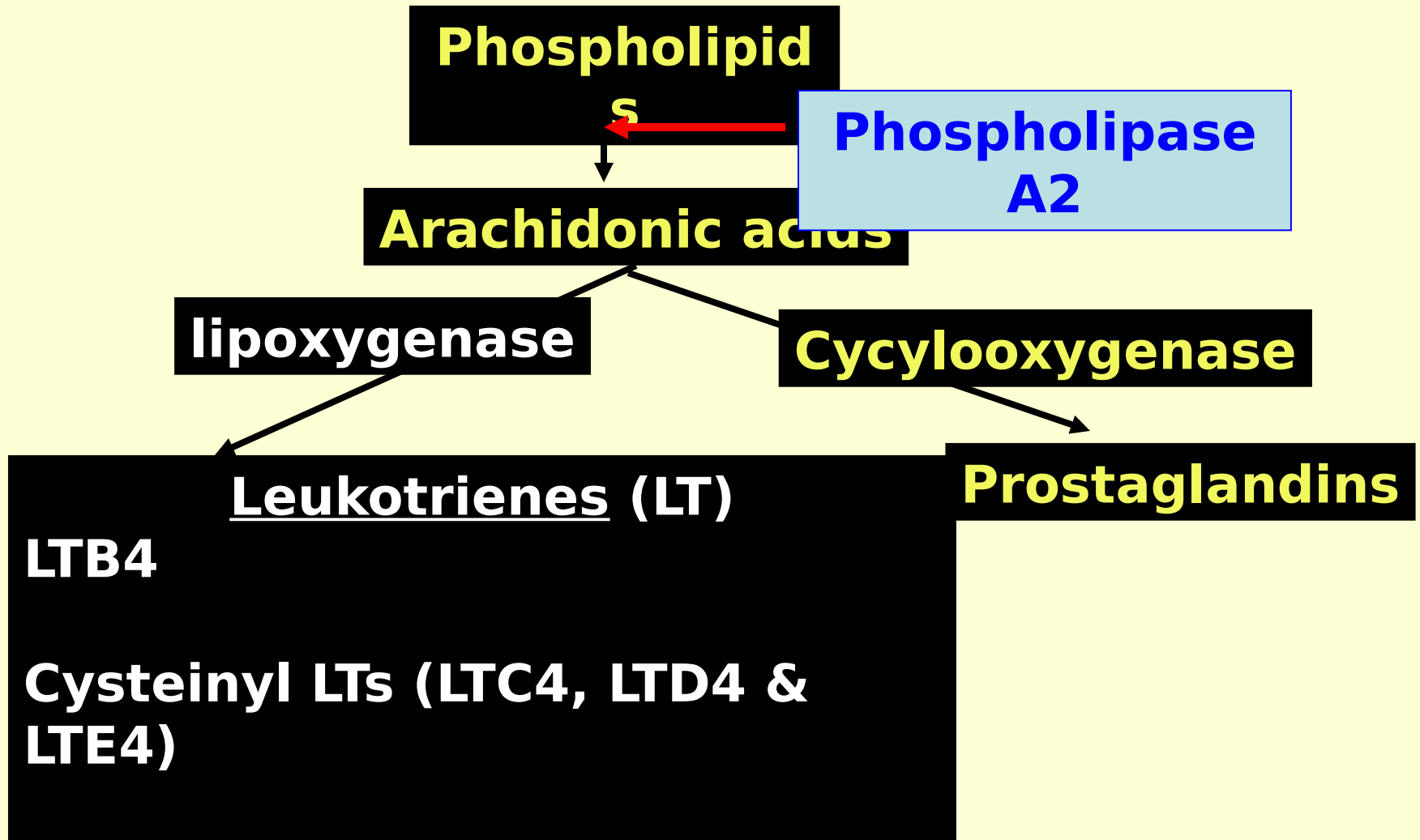
2-Which of the following is considered a side effect of The inhaled corticosteroids used in the treatment of bronchial asthma?

- a) Vertigo
- b) Dizziness
- c) Fainting
- d) Dysphonia
- e) Dry cough



Leukotriene Modifiers





■ **LTB4** is a potent chemo-attractant for neutrophils and eosinophils.

■ **Cysteinyl leukotrienes :**

- constrict bronchiolar smooth muscle
- increase endothelial permeability
- promote mucus secretion

■ **Zileuton**

is a **selective inhibitor of 5-lipoxygenase**

preventing the formation of both LTB4 and the cysteinyl

LTs

■ **Zafirlukast & Montelukast**

They are **selective antagonists** of the cysteinyl leukotriene-1 receptor

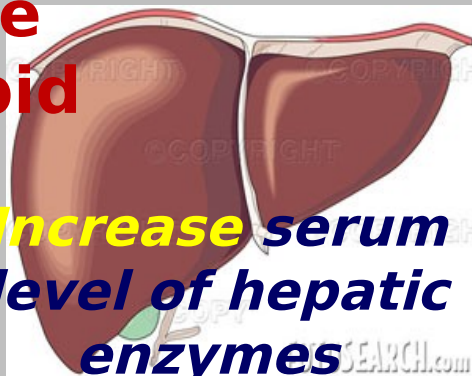
■ All three drugs are approved **for the prevention of**
asthma symptoms.



Cell
membrane
phospholipid



*Increase serum
level of hepatic
enzymes*



**Leukotriene
Modifier**

Arachidonic acid

C.O.

PG

L.O.X

LT

Zileuton

Montelukast

Zafirlukast

R

Zafirlukast & Zileuton

are inhibitors of
cytochrome P450

**Bronchodilation
Inflammation**



3-Which of the following is a selective antagonist of the cysteinyl leukotriene-1 receptor and could also inhibits cytochrome P450 enzymes?

- a) Nedocromil
- b) Zafirlukast
- c) Montelukast
- d) Omalizumab
- e) Cromolyn



Key Points Summary

❑ ***Corticosteroids are antiinflammatory drugs used by :***

- *Inhalation: in prophylaxis of asthma*
- *IV infusion: in acute severe asthma*
- *Oral : In resistant asthma*

Side effects dysphonia and oro- pharyngeal candidiasis and could be avoided ??

❑ ***Leukotrien modifiers : ORAL***

- *Anti-inantiinflammatory drugs used in prophylaxis of asthma*

Leukotriene receptor antagonists & lipoxgenase inhibitor

Zafirlukast & Zileuton are inhibitors of cytochrome P450

SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.





Thank You

